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The objective of the proposed research is to develop computer-aided diagnosis methods for use in mammography in order to increase the diagnostic accuracy of radiologists. Specifically we have developed advanced computerized schemes for the detection spiculated lesions and architectural distortions based on the calculation of the Hough spectrum and for the detection of small, low-contrast early cancers based on gradient and circularity filters. Also, computerized classification schemes for masses using artificial neural networks, rule-based methods, and hybrid systems have been developed. We also investigated a computerized method for including temporal change between mammographic examinations. The efficacy and efficiency of the CAD methods for mammography are being evaluated on a clinical workstation. The potential significance of this research project lies in the fact that if the detectability of cancers can be increased by employing a computer to aid the radiologist's diagnosis, then the treatment of patients with cancer can be initiated earlier and their chance of survival improved.

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INTRODUCTION

Nature of the problem

Breast cancer is a leading cause of death in women, causing an estimated 44,000 deaths per year. Mammography is the most effective method for the early detection of breast cancer and it has been shown that periodic screening of asymptomatic women does reduce mortality. Mammography is becoming one of the largest volume x-ray procedures routinely interpreted by radiologists.

Although mammography is currently the best method for the detection of breast cancer, between 10-30% of women who have breast cancer and undergo mammography have negative mammograms. In approximately two-thirds of these false-negative mammograms, the radiologist failed to detect the cancer that was evident retrospectively. Low conspicuity of the lesion, eye fatigue and inattentiveness are possible causes for these misses. We believe that the effectiveness (early detection) and efficiency (rapid diagnosis) of screening procedures could be increased substantially by use of a computer system that successfully aids the radiologist by indicating locations of suspicious abnormalities in mammograms.

In addition, many breast cancers are detected and referred for surgical biopsy on the basis of a radiographically detected mass lesion or cluster of microcalcifications. Although general rules for the differentiation between benign and malignant breast lesions exist, considerable misclassification of lesions occurs with the current methods. On average, only 10-30% of masses referred for surgical breast biopsy are actually malignant. Surgical biopsy is an invasive technique that is an expensive and traumatic experience for the patient and leaves physical scars that may hinder later diagnoses (to the extent of requiring repeat biopsies for a radiographic tumor-simulating scar). A computerized method capable of detecting and analyzing the characteristics of benign and malignant masses, in an objective manner, should aid radiologists by reducing the numbers of false-positive diagnoses of malignancies, thereby decreasing patient morbidity as well as the number of surgical biopsies performed and their associated complications.

The development of computer methods to assist radiologists is a timely project in the sense that digital radiography is on the threshold of widespread clinical use. The arrival of digital radiographic systems allows for the acquisition of image data in a format accessible to computerized schemes. The potential significance of this research project lies in the fact that if the detectability of cancers can be increased by employing a computer to aid the radiologist's diagnosis, then the treatment of patients with cancer can be initiated earlier and their chance of survival improved.

Background of previous work

Breast cancer is a leading cause of death in women, causing an estimated 44,000 deaths per year (1). Mammography is the most effective method for the early detection of breast cancer (2-5) and it has been shown that periodic screening of asymptomatic women does reduce mortality (6-11). Various medical organizations have recommended the use of mammographic screening for the early detection of breast cancer (3). Thus, mammography is becoming one of the largest volume x-ray procedures routinely interpreted by radiologists.

It has been reported that between 30 to 50% of breast carcinomas detected mammographically demonstrate clusters of microcalcifications (12-14), although about 80% of breast carcinomas reveal microcalcifications upon microscopic examination (15-18). In addition, studies indicate that 26% of nonpalpable cancers present mammographically as a mass while 18% present both with a mass and microcalcifications (19). Although mammography is currently the best method for the detection of breast cancer, between 10-30% of women who have breast cancer and undergo mammography have negative mammograms (20-24). In approximately two-thirds of these false-negative mammograms, the radiologist failed to detect the cancer that was evident retrospectively (23-26). Low conspicuity of the lesion, eye fatigue and inattentiveness are possible causes for these misses. It has been suggested that double reading (by two radiologists) may increase sensitivity (27-29).We believe that the effectiveness (early detection) and efficiency (rapid diagnosis) of screening procedures could be increased substantially by use of a computer system that successfully aids the radiologist by indicating locations of suspicious abnormalities in mammograms.

Many breast cancers are detected and referred for surgical biopsy on the basis of a radiographically detected mass lesion or cluster of microcalcifications. Although general rules for the differentiation between benign and malignant breast lesions exist (20,30), considerable misclassification of lesions occurs with the current methods. On average, only 10-30% of masses referred for surgical breast biopsy are actually malignant (20,31). Surgical biopsy is an invasive technique that is an expensive and traumatic experience for the patient and leaves physical scars that may hinder later diagnoses (to the extent of requiring repeat biopsies for a radiographic tumor-simulating scar). A computerized method capable of detecting and analyzing the characteristics of benign and malignant masses, in an objective manner, should aid radiologists by reducing the numbers of false-positive diagnoses of malignancies, thereby decreasing patient morbidity as well as the number of surgical biopsies performed and their associated complications.

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Work of others in the field

Comprehensive summaries of investigations in the field of mammography CAD have been published by the P.I. (30,31). In the 1960's and 70's, several investigators attempted to analyze mammographic abnormalities with computers. Winsberg et al. (34), in an early study, examined areas of increased density in contralateral breasts. They felt that their results 35) developed various feature-extraction techniques and a two-view verification method involving medio-lateral oblique and cranio-caudal views to detect microcalcifications. Kimme et al. (36) developed a computerized method for the detection of suspicious abnormalities in mammograms based on the statistical measures of textural features. A similar approach using texture analysis and bilateral comparison was also employed by Hand et al (37) and Semmlow (38) in the computerized localization of suspicious abnormal areas of breasts. Their results yielded a 66% true-positive rate with approximately 26 false

suspicious areas per image. With regard to classification methods, Ackerman et al. (39), using digital xeroradiographs, devised four measures of malignancy: calcification, spiculation, roughness and shape, to perform classification on specific areas selected by human observers. The same group (40) did, however, attempt to improve diagnosis by using 36 radiographic properties which were evaluated semi-quantitatively by a radiologist for input to a computer decision tree. Wee et al. (41) and Fox et al. (42) performed preliminary studies on the classification of microcalcifications. These previous studies demonstrated the potential capability of using a computer in the detection of mammographic abnormalities.

Computer-aided diagnosis, in general, has attracted little attention twenty years ago, perhaps due to the inconvenience involved in obtaining a radiograph in digital format. Recent work, though, shows a promising future. Magnin et al. (43) and Caldwell (44) used texture analysis to evaluate the breast's parenchymal pattern as an indicator of cancer risk. These preliminary studies raised many unanswered questions regarding topics ranging from the digital recording process to the type of numerical risk coefficient employed. Thus, further studies using texture analysis are indicated. The work by Fam and Olson (45,46) on the computer analysis of mammograms is encouraging; however, their method has only been tested on 20 mammographic regions of interest (each roughly half a mammogram). Davies and Dance (47) have reported on their automatic method for the detection of clustered calcifications using local gray-level thresholding and also a clustering rule. Their results yielded a true-positive rate of 96%; however, no indications of the subtlety and size of the calcifications were given. Astley et al. (48), Grimaud et al. (49) and Mascio et al. (50) reported on their methods for the detection of breast lesions. Karssemeijer (51) has described a stochastic method based on Bayesian decision theory that appears promising. Lai et al. (52) and Brzakovic et al. (53) are also developing techniques for the detection of mass lesions. The actual performance level and difficulty of the databases, however, are unknown. Kegelmeyer (54) has demonstrated a technique for the detection of stellate lesions. Gale et al. (55) and Getty et al. (56) are both developing computer-based classifiers, which take as input diagnostically-relevant features obtained from radiologists' readings of breast images. Getty et al. found that with the aid of the classifier, community radiologists performed as well as unaided expert mammographers in making benign-malignant decisions. Swett et al. (57,58) are developing an expert system to provide visual and cognitive feedback to the radiologist using a critiquing approach combined with an expert system.

Previous relevant work of the investigators

We in the Kurt Rossmann Laboratories for Radiologic Image Research at The University of Chicago have vast experience in developing various computer-aided diagnosis (CAD) methods in mammography, chest radiography, and angiography (59-86). Our CAD methods in digital mammography, which include the computerized detection of microcalcifications and masses, have achieved useful levels of sensitivity and specificity and thus are currently undergoing clinical testing.

Computerized detection of clustered microcalcifications

Our detection scheme for clustered microcalcifications includes a preprocessing step referred to as a difference-image approach (59,60). Basically, the original digital mammogram is spatially filtered twice: once to enhance the signal-to-noise ratios of the microcalcifications and a second time to suppress them. The difference between the two resulting processed images yields an image (a difference image) in which the variations in background density are largely removed. Microcalcifications are then segmented from the difference image using global gray-level thresholding and local thresholding techniques. The segmented image is next subjected to feature-extraction techniques in order to remove signals that likely arise from structures other than microcalcifications, including size analysis, texture analysis, and clustering analysis (62-65,76,85). In addition, a shift-invariant neural networks is used directly on the digital image data in order to enhance microcalcifications and reduce false-positive detections.

The computerized scheme for detection of clustered microcalcifications (61) developed at The University of Chicago has been tested as an aid to radiologic diagnosis. Radiologist detection performance was evaluated using ROC (receiver operating characteristic) methodology (87). It was found from the ROC analysis that there was a statistically significant improvement in the radiologists' accuracy when they were given the computer-generated diagnostic information (at either false-positive level), compared with their accuracy obtained without the computer output.

Computerized detection of masses

Our initial method for the detection of mammographic masses is based on deviations from the architectural symmetry of normal right and left breasts, with asymmetries indicating potential masses (66-68,74). The input to the computerized scheme, for a given patient, are the four conventional mammograms obtained in a routine screening examination: the right cranio-caudal (CC) view, the left CC view, the right medio-lateral-oblique (MLO) view, and the left MLO view. After automatic registration of corresponding left and right breast images, a nonlinear subtraction technique is employed which includes a run-length analysis to yield two images that contain locations of suspected masses for the left and right breasts (75). Next, feature-extraction techniques, which include morphological filtering and analysis of size, shape and distance from border, are used to reduce the number of false-positive detections. These features are merged using an artificial neural network.

Use of artificial neural networks for detection and classification

We have also investigated the application of artificial neural networks to the detection and classification of mammographic lesions. We used an artificial neural network (ANN) to extract microcalcification image data from digital mammograms (65). The ANN, which was supplied with the power spectra of remaining suspected regions (from the CAD scheme) as input, distinguished actual clustered microcalcifications from false-positive regions and was able to eliminate many of the false positives. Also, we are applying ANNs to the decision-making task in mammography (69). Three-layer, feed-forward neural networks with a back-propagation algorithm were trained for the interpretation of mammograms based on features extracted from mammograms by experienced radiologists. The database for input to the ANN consisted of features extracted from 133 textbook cases and 60 clinical cases. Performance of the ANN was evaluated by ROC analysis. In tests, using 43 initial image features (related to masses, microcalcifications and secondary abnormalities) that were later reduced to 14 features, the performance of the neural network was found to be higher than the average performance of attending and resident radiologists in classifying benign and malignant lesions. At an optimal threshold for the ANN output value, the ANN achieved a classification sensitivity of 100% for malignant cases with a false-positive rate of only 41%, whereas the average radiologist yielded a sensitivity of only 89% with a false-positive rate for classification of 60%.

Pre-clinical testing of an "intelligent" mammography workstation

We have implemented our computerized detection schemes for masses and clustered microcalcifications on a prototype "intelligent" mammography workstation in an ongoing clinical study (70,72,85). The workstation, on which the automated computerized detection schemes are run, consists of a film digitizer, a high-speed computer, a magneto-optical jukebox, and hard and soft copy displays. Preliminary prospective evaluations of the prototype, which was installed in the clinical mammography reading area at the University of Chicago Medical Center on November 8, 1994, are promising.

Computerized classification of mammographic masses

Malignant masses often can be distinguished from benign masses due to their more spiculated appearance in the mammographic image. Thus, in the classification of masses, our computerized scheme is based on the degree of spiculation exhibited by the mass in question (77,82). The mass is first extracted from the anatomic background of the mammogram using region-growing techniques. After a mass is isolated from the background, its margin information is extracted. This margin is then smoothed in order to substantially reduce possible spicules. The difference before and after the smoothing operation provides an indicator of the degree of margin spiculation, with a large difference

corresponding to a high degree of spiculation and therefore, a greatly increased likelihood of malignancy. We developed a method for the automated extraction of the lesion from the parenchymal background in order to facilitate the extraction of various features (82). The features extracted were obtained from cumulative edge gradient histogram analysis, which we originally developed for analyzing lung nodules (88), however, the gradient was analyzed relative to the radial angle. Other features included gray-level measures and geometric measures. In the cumulative edge-gradient analysis, the maximum gradient and angle of this gradient relative to the radial direction is calculated. From the cumulative edge-gradient-orientation histogram, various measures are calculated including FWHM (full-width at half-max), standard deviation of the cumulative edge gradient and average gradient in the radial direction. With a pathologically-confirmed database of 95 masses (57 malignant and 38 benign), the classification scheme achieved an A_Z (area under the ROC curve) of 0.90 using a rule-based scheme together with a conventional feed-forward back-propagation neural network.

The Mammo/Icon system

Dr. Swett's group began investigating methods for strengthening radiologic diagnosis in conjunction with Dr. Perry Miller. They developed an expert system called ICON which was able to generate context sensitive English prose critiques containing advice about radiologic diagnosis (57). One of the lessons learned during this project was that a great deal of radiologic decision making primarily involves visual pattern recognition rather than formal cognitive analysis. They therefore investigated methods to reinforce this kind of visual reasoning which culminated in the development of a new system called Image/Icon (58). This system supplements critiques with display of reference images selected to confront issues raised by a given clinical case. Inspection of reference images often allows the radiologist to confirm a suspected diagnosis, or consider other diagnostic possibilities. Special retrieval and display strategies have been developed to further strengthen visual reasoning by organizing retrieved images in diagnostically relevant ways. These concepts were primarily developed in a system dealing with the mammographic diagnosis of breast cancer known as Mammo/Icon . Mammo/Icon has been designed to compliment a radiologists normal reading patterns. The system is used to report mammographic findings, using either speech recognition technology, or mouse interaction with a graphical user interface. As findings are recorded, Mammo/Icon functions in the background, collecting potentially helpful images from a knowledge base. In this proposal, we plan to modify the Mammo/Icon system so that the features of the lesion in question are automatically determined. The system would then automatically retrieve images of similar characteristics for display to the radiologist. Along with the images, the computer would also indicate an estimate of the likelihood of malignancy.

Purpose of the present work

The main hypothesis to be tested is that given dedicated computer-vision programs for the computer-assisted interpretation of mammograms, the diagnostic accuracy for mammographic interpretation will be improved, yielding earlier detection of breast cancer (i.e., a reduction in the number of missed lesions) and a reduction in the number of benign cases sent to biopsy. Computer-aided diagnosis (CAD) can be defined as a diagnosis made by a radiologist who takes into consideration the results of a computerized analysis of radiographic images and uses them as a "second opinion" in detecting lesions and in making diagnostic decisions. The final diagnosis would be made by the radiologist.

Methods of approach

The objective of the proposed research is to develop computer-aided diagnosis methods for use in mammography in order to increase the diagnostic decision accuracy of radiologists and to aid in mammographic screening programs. The CAD methods will include a parallel method for the detection of a range of mass types and for the incorporation of information from multiple views (i.e., CC and MLO, and prior mammograms).

The **specific objectives** of the research to be addressed are:
(1) Development of advanced computerized schemes for the detection and classification of masses in digital mammograms.
(a) Development of a computerized detection scheme for spiculated lesions and architectural distortions based on the calculation of the Hough spectrum.
(b) Development of a computerized detection scheme for small, low-contrast early cancers based on gradient and circularity filters.
(c) Incorporation of the two new methods with a previously-developed bilateral-subtraction method along with feature analyses into a system for lesion detection.
(d) Further development of computerized classification schemes for masses.
(2) Development of computerized methods based on multiple views for enhanced mammographic interpretation.
(a) Development of computerized methods for the incorporation of image information from the CC and MLO views of mammographic examinations.
(b) Development of computerized methods for analysis of temporal change between mammographic examinations.
(3) Incorporation of the computer-vision methods with an Mammo/Icon mammographic review system for enhanced diagnosis.
(a) Expansion of the Mammo/Icon database descriptors to include CAD derived parameters.
(b) Calculation of the computer extracted features of images in the Mammo/Icon database.
(c) Development of hardware and software interfaces for CAD and Mammo/Icon.
(4) Evaluation of the CAD methods for mammography.

BODY: Experimental methods and results to date

Development of advanced computerized schemes for the detection of masses in digital mammograms.

Experimental methods

Additional detection methods for masses are needed due to the variation in types of masses. Our current bilateral-subtraction method has been shown to be successful in the detection masses that are apparent from the deviation from symmetry between the left and right breasts. However, very spiculated lesions and architectural distortions are not always detected with the bilateral subtraction method and very small, low-contrast cancer lesions also are difficult to detect using the bilateral subtraction method.

For each digital mammogram, prior to the computer analysis for the detection of lesions, it is necessary to identify the breast region from the rest of the film regions. The breast region will be automatically segmented by excluding uniform dark (direct exposure) and uniform bright (unexposed) film regions. Initial noise filtering using a median filter will be applied to the digital image followed by application of a gray-value range operator (80). Using information from the local range operator a modified global histogram analysis will be performed. Region growing will be performed on the threshold image, followed by a morphological erosion operation. A distance map of the image will be determined and the boundary of the segmented object in the image will be then tracked to yield its contour. The contour will then be used in the subsequent image analysis schemes. Our initial evaluation of this segmentation algorithm involved the analysis of 740 digital mammograms with a resulting 97% of the detected contours acceptable for CAD usage (79).

We are developing methods for the segmentation of dense portions in the breast since such regions can obscure the visibility of lesions and distortions. Determination of the dense portions within the breast region is done using gray-level histogram analysis within the breast region as well as within a small region along the chest wall. This selection of ROI location is due to the fact that as one approaches the chest wall within a mammogram, the amount of dense tissue decreases, and thus an estimation of the pixel value corresponding to fatty tissue can be calculated. The ROI, of predetermined width and height is positioned at a predetermined distance (mm or pixels) from the chest wall. The location of the chest wall side in the mammogram is determined during the breast segmentation step since it differs greatly from the external side of the breast. By analysis of the bimodal nature of the histograms, a peak will be located corresponding to the dense region cutoff. Gray-level thresholding within the breast region is then performed. Thus, the ROI near the chest wall, as compared to that of the entire breast regions can be used to indicate the gray levels of the fatty portions. With a database of 700 mammograms, the dense portions as segmented by the computer and those segmented by a radiologist had good correlation at a statistical significant level.

Mammographic spiculated lesions and architectural distortions are usually associated with malignancy, which makes them important signs in the screening of breast cancer. Presented here is a novel method for the automatic detection of these lesions with the use of a Hough spectrum-based geometric texture analysis. The Hough spectrum technique is developed from the traditional Hough transform, which is effective in the description of geometric structures. For our investigation, Hough spectra will be calculated for regions-of-interest (ROIs) within the breast region of the digitized mammogram (84). Thresholding will then be conducted with the threshold level based on the statistical properties of the spectra. Those ROIs with strong signals of spiculation or architectural distortion will be indicated as regions of potential lesions. We will also investigate the effect of ROI size on performance.

Hough transform stems from the very general format of object description with:

$$f(\vec{x},\vec{a}) = 0 \qquad (1)$$

where $\vec{x} = (x_1,x_2,\cdots,x_n)^T$ is a set of variables and $\vec{a} = (a_1,a_2,\cdots,a_m)^T$ a set of parameters. Both may form a space of an appropriate dimension, which could be termed as spatial domain and parameter domain respectively. The description of many basic geometric elements, such as straight lines, circles, parabolas (123-124) takes the form of Eq.(1). For example, under the so-called normal parameterization, a straight line can be described by:

$$\rho = x\cos\theta + y\sin\theta \qquad (2)$$

where ρ is the length of the normal segment from the origin to the line, and θ is the angle of this normal. The Hough transform maps this line to a single point at (ρ,θ) of the $P-\Theta$ parameter domain. On the other hand, every point in the geometric space corresponds to a curve in the parameter domain according to Eq.(2), and the crosspoint of two such curves corresponds to a straight line in the spatial domain that is determined by the two corresponding points. Therefore, the colinearity in the original image can be examined through Hough transform by observing the accumulation on the number of passing curves at each possible crosspoint position in the parameter domain. Also, the Hough transform of a family of corradial lines is a group of points lying on one and the same sinusoidal curve. This dual property of the point-to-curve transformation forms the foundation of the Hough transform in geometric elements' detection.

Assume that $f(x,y)$ $(x,y = 0,1,\cdots,N-1)$ is the original image, and $h(u,v)$ $(u = 0,1,\cdots,M_h;\ v = 0,1,\cdots,N_h)$ denotes the outcome of the transformation. Now line up both $f(x,y)$ and $h(u,v)$ by rows (or columns) separately into column vectors $\vec{\xi}$ and $\vec{\zeta}$,:

$$\vec{\xi} = \begin{bmatrix} \xi_1 \\ \vdots \\ \xi_k \\ \vdots \\ \xi_{N^2} \end{bmatrix} \qquad (3)$$

$$\vec{\zeta} = \begin{bmatrix} \zeta_1 \\ \vdots \\ \zeta_l \\ \vdots \\ \zeta_{M_h \times N_h} \end{bmatrix} \qquad (4)$$

so that:

$$\xi_k = f(x,y) \qquad (5)$$

$$\zeta_l = h(u,v) \qquad (6)$$

where:

$$k = xN + y + 1 \qquad (7)$$

$$l = uN_h + v + 1 \qquad (8)$$

Then, the Hough transform can be expressed in terms of matric algebra as follows:

$$\vec{\zeta} = A\vec{\xi} \qquad (9)$$

where $A = [a_{lk}]_{N^2 \times M_h N_h}$ is a 0-1 matrix. Its element a_{lk} is one if the signal at point ξ_k should be accumulated at position ζ_l, and zero otherwise.

The accumulation in Hough transform is fulfilled in Eq.(9) by matric multiplication. Here, $\vec{\zeta}$ is referred to as the Hough spectrum. This, however, is not merely a name assigned to the output of the traditional Hough transform. There are no specific preprocessing requirements on image $\vec{\xi}$. For

instance, it needs not to be a binary edge image of the original data, as were the cases where Hough transform were typically applied. In addition, matrix A depicts the transformation which is induced by each and every pixel of the original image.

Just as in the case of traditional Hough transform, the useful information in a Hough spectrum lies in its accumulated peaks. Therefore each Hough spectrum should be thresholded first before any further analysis. The threshold used in this study is determined based on statistical properties of Hough spectrum's magnitude function

The radiographic appearance of the breast tissue is abundant in the textural information composed of bright and slender unite structures. Generally, the distribution of these textural element takes the pattern of radiating from nipple to the chest wall, which makes them roughly parallel to one another locally. The presence of certain abnormal structures such as a spiculated mass or an architectural distortion, however, may alter this trend by generating another radiating center, thus changes the textural appearance dramatically in a neighboring area. The basic structural unit of the mammographic textural pattern can be modeled as stripe. Hence, the technique can be applied to analyze the mammographic textural pattern, especially for the detection of the above mentioned abnormal structures. In the Hough-spectrum-based analysis, ROIs are placed within the breast region of the digitized mammogram and from the image data within each ROI a Hough spectrum is calculated (87).

In addition, with screening mammography, an increasing number of small invasive breast cancers is found, which can be seen on mammograms as small circumscribed mass often < 1 cm. Current computer-aided detection schemes based on bilateral subtraction are not well suited for these small masses, due to significant normal variations between the right and left breast . The purpose of this task is to develop a single-image method specifically for the computer-aided detection of small circumscribed masses. The method, we are developing, is based on a modified median filter, a modified morphological open operation, filtering with a mass filter for the initial detection of circumscribed densities, matching using a deformable shape template with Fourier descriptors, characterization of the match using simulated annealing, and measuring the circularity and density characteristics of the suspected lesion. After a 3x3 median filtering step, a morphological open (erosion followed by dilation) operation with a 7 pixel wide circle as structuring element is used to eliminate small circular and thin linear structures below a certain diameter (83). To preserve the gray value characteristics of larger lesions as far as possible, only pixels with a small difference to the local minimum are used as erosion centers. If the gray value after dilation exceeds the original pixel value, the original pixel value is used instead of the filtered value.

A newly designed second derivative filter with a circular, 21-pixel wide base identifies circumscribed density peaks in the image. The filter value is based on the local gradient (7x7 kernel) in x- (D_x) and y- (D_y) direction. The edge orientation at a specific image point is equivalent to the gradient vector $\begin{pmatrix} D_x \\ D_y \end{pmatrix}$ and the edge strength is calculated as the second derivative in edge orientation. This assures that regions with a constant gradual slope do not contribute to the filter value. The filter value is first calculated separately for 16 edge orientation bins γ.

$$\mathbf{f}(\gamma) = \frac{1}{N} \sum_{P \in K} \begin{cases} 0, \text{ if edge orientation}(P) \notin \gamma \\ \\ \text{MAX}(0, \cos\varphi) * \text{edge strength}(P), \text{ if edge orientation}(P) \in \gamma \end{cases}$$

$f(\gamma)$ filter value for edge orientation bin γ
K filter kernel
P neighbor point in K
N number of points in K
φ angle between gradient vector and connection line center point/neighbor point

The final filter value is then calculated as the sum of the individual orientation bins with omission of the 4 bins with the highest values:This prevents an influence of straight edges (e.g. the pectoralis muscle border) on the filter value without changing the filter value for ideal circular lesions. Local maxima of the filter value define potential center positions of mass lesions, which are used in the next step, the matching of a deformable template onto the lesion border. In this process, a deformable shape template is created by inverse Fourier transform of a limited number of complex Fourier terms. The final lesion contour is then identified by variation of the Fourier terms within a certain range with minimization of a cost function based on lesion contrast and edge strength using simulated annealing.

For further characterization, a rectangular ROI containing the lesion is extracted from the original peripheral density corrected image. This is used to calculate lesion size, lesion contrast and a radial gradient index RGI, defined as follows:

$$\mathbf{RGI} = \frac{\sum_{P \in L} \cos\varphi \sqrt{D_x^2 + D_y^2}}{\sum_{P \in L} \sqrt{D_x^2 + D_y^2}}$$

RGI radial gradient index $-1 \le RGI \le 1$
P image point
L detected lesion excluding the center part
D_x gradient in x-direction
D_y gradient in y-direction
φ angle between gradient vector and connection line from center point to neighbor point

The RGI is a measure of the circularity and density characteristics of a lesion and approaches 1.0 for a ideal circular lesion. It is used to differentiate between true and false positive detections. The algorithm is used repetitively at different resolutions with the pixel size varying from 0.5 mm to 4 mm. Each resolution step covers a certain range of lesion sizes. In the final step, the different detected lesions are integrated into one final result. In case of overlap between different detected lesions, the lesion with the smaller radial gradient index is eliminated.

Output from the three detection preprocessing methods (i.e., the bilateral-subtraction technique, the Hough-spectrum-based technique and the gradient/circularity filter technique) will be merged. The output from each method will go through its own feature analysis method in order to reduce false positives. We currently have 90 features that can be calculated for a suspect lesion both at high resolution (0.1 mm pixel size) and at low resolution (0.5 mm pixel size). We will determine which features are appropriate for each of the three preprocessing methods. These features will be selected based either on one-dimensional analysis (86) or on multi-dimensional analysis involving genetic algorithms (89). False positive reduction will occur based solely on the type of preprocessing methods which will enhance the abnormality. Further reduction in false-positive detections will occur during the feature-analysis stage. In the feature-analysis stages, regions deemed suspicious by the method will be subjected to geometric-based measures, intensity-based measures, edge-gradient-orientation methods and texture-based measures. (82,86,89). We have successfully developed and used these various types of features to reduce false-positive detections in our other CAD schemes. We realize, of course, that features and the combination of such features used for reducing false positives in mass detections schemes will differ in the proposed scheme for spiculated lesions and architectural distortions. Features used will depend on the specific type of false positives generated by the specific method. It should be noted that false positives generated by the Hough-spectrum-based method may differ from those generated by the bilateral subtraction method and by the gradient/circularity method.

We will evaluate artificial neural networks (ANN) as a means to merge the various features obtained from the computer analysis of the mammograms [in a manner we have successfully used in

the past for merging mammographic feature data (69)]. The various features will serve as input data and will be supplied to the input units of the neural network. Prior to input to the ANN, the features will be normalized between 0 and 1. The output data from the neural network are then obtained through successive nonlinear calculations in the hidden and output layers. The calculation at each unit in a layer includes a weighted summation of all entry numbers, an addition of a certain offset number, and a conversion into a number ranging from 0 to 1 using a sigmoid-shape function such as a logistic function. The neural network will be trained by a back-propagation algorithm using pairs of training input data and desired output data. The desired output data will be initially 1 if the suspect lesion is an actual lesion and 0 otherwise. Once trained, the neural network will accept features and output a value will be related to the likelihood of being an actual lesion (i.e., a true-positive). Feature selection will be performed by analyzing the average and standard deviation of the various features for both high and low risk subjects. Az values will be calculated for each feature as well as for the output of the ANNs. In addition, genetic algorithms, which we have used, in a pilot study, for optimizing feature selection for the task of distinguishing true-positive and false-positive mass detections, will also be used (89).

In the parallel system, images will be analyzed by all three computerized detection methods and the output from each will be merged in a single result file. During grouping either the ANN output value from each detection method will be input to a "grouping" ANN or a logical OR operation followed by a distance grouping operation will be performed. The "grouping" ANN will take as one input a zero value if, for example, only two of the three detection methods identify a suspicious region. In the logical OR operation the sensitivity will increase, but so will the false-positive rate, and thus, the subsequent grouping operation is necessary. In the grouping operation, if two detections are within a specific distance from each other, than the locations will be merged to yield a single identification. The training of these operations will be performed as discussed for other ANNs above. We currently use a grouping operation for the output of the bilateral subtraction method.

Results to date

As of March 1997, over 9500 cases have been analyzed for computerized detection on our clinical prototype mammography worstation. We are analyzing the sensitivity and false-positive rate of the intelligent workstation for the first two-years of implementation: November 8, 1994 to November 7, 1996, which includes 8035 mammographic screening cases. Thirty-five cancers have been confirmed to date within this 2-year period, with one case yielding a negative mammogram but with a palpable lesion. Twenty-three of the 34 cancers were detected by the computer (16 of 23 cases containing masses and 7 of 13 cases containing clustered microcalcifications.) Nine of the patients with cancer had 2 screening exams during the two-year period. In three of the nine cases, the computer indicated the region in the first exam where the cancer was subsequently diagnosed by the radiologist in the second exam. The computer output contains, on average, 0.9 false-positive microcalcification clusters and 1.4 false-positive masses. The types of false-positive detections found by the computer in mass detection and clustered microcalcification detection were investigated for 1296 cases. Of the false positives that were indicated by the computer, over 80% of the mass false positives were due to nodular densities on the film. In order to determine the effect of false-positive detections on mammographic interpretation, we calculated the call-back rate in one-year time periods before and after implementation of the workstation in the clinical area. The callback rate is the fraction of screening mammograms read as abnormal. Before introduction of CAD, 13.2% of screeners were called back for further workup and after the introduction of CAD, 12.6% of screeners were called back for further workup. Thus, the false-positive output from the computer did not increase the number of women called back.

With the single-image method for detection of small invasive breast cancers (83) localized density peaks on mammograms are identified using a gradient/circularity filter. Lesion contours were generated by matching a deformable template onto a second derivative edge map. In a preliminary study (without further feature analyses to reduce false positives) using 45 non-palpable invasive

breast cancers, all with a size less than 1 cm (median size of 7 mm), 82% of the cancers were detected with an average false-positive rate of 2.8 per image (104).

In the Hough spectrum geometric texture analysis technique, the mammogram is analyzed ROI by ROI (84). Each ROI is transformed into its Hough spectrum and then thresholding is performed with its threshold level based on the statistical properties of the spectrum. ROIs with strong signals of spiculation are then screened out as regions of potential lesions. In a preliminary study, 32 images containing spiculated lesions/architectural distortions (biopsy confirmed) were analyzed using information extracted from the Hough spectrum. Our preliminary studies, using only the Hough spectrum based technique without further feature analyses to reduce false positives, yielded sensitivities of 81% for spiculated masses and 67% for architectural distortions at false positives rates of 0.97 and 2.2 per image, respectively (105). We have also converted the method into a parallel program to expedite the development and optimization of the parameters such as ROI size.

Output from the bilateral subtraction method and that of the gradient/circularity filtering were combined and analyzed. Many masses were detected by both preprocessing methods. For a database of 20 cancer cases, the bilateral yielded a sensitivity of 75% (at 1.8 false-positives detections per image) and the gradient/circularity filter yielded a sensitivity of 70% at the same false postivie rate. Upon comparison, the gradient/circularity filter found masses that the bilateral did not, thus allowing the sensitivity to increase to 80%. We are currently comparing the false positive overlap to determine the false-positive rate for the combined scheme as well as give us a means to improve the false-positive rate while optimizing the sensitivity for each method.

Development of advanced computerized schemes for the classification of masses in digital mammograms.

Experimental methods

Spiculation is a primary sign of malignancy for masses detected by mammography. We have developed a technique that analyses patterns and quantifies the degree of spiculation present (82). Our current approach involves (1) automatic lesion extraction using region growing and (2) feature extraction using radial edge-gradient analysis. Two spiculation measures are obtained from an analysis of radial edge-gradients. These measures are evaluated in four different neighborhoods about the extracted mammographic mass. The performance of each of the two measures of spiculation was tested on a database of 95 mammographic masses using ROC analysis that evaluates their individual ability to determine the likelihood of malignancy of a mass. The dependence of the performance of these measures on the choice of neighborhood was analyzed. We have found that it is only necessary to accurately extract the approximate outlines of a mass lesion for the purposes of this analysis since the choice of a neighborhood that accommodates the thin spicules at the margin allows for the assessment of margin spiculation with the radial edge-gradient analysis technique. Two promising measures are the FWHM and the average radial gradient which correspond to the degree of spiculation and how ill-defined is the margin, respectively. The two measures performed at their highest level when the surrounding periphery of the extracted region is used for feature extraction, yielding A_z values of 0.83 and 0.85, respectively, for the determination of malignancy. These are similar to that achieved when a radiologist's ratings of spiculation (A_z=0.85) are used alone. The maximum value of one of the two spiculation measures (FWHM) from the four neighborhoods yielded an A_z of 0.88 in the classification of mammographic mass lesions.

In this objective, we plan to use artificial neural networks along with other measures of the mass in question to obtain an estimate of the likelihood of malignancy. The margin, shape and density of a mass are the three major characteristics used by radiologists to classify mass lesions. Among the three, margin characteristics of a mass are considered to be the most important indicators of its benign and malignant status. The margin of a mass can be categorized as circumscribed, microlobulated, obscured, indistinct or spiculated with a spiculated margin being the strongest sign of malignancy.

After the margin of a mass is accurately identified, seven features related to the margin, shape and density of a mass will be extracted from the neighborhoods of the identified mass region: three of them provide margin information; one is used to describe the shape of the mass; the rest are extracted to estimate the density of the mass. Margin information will be obtained.

The shape of a mass can be described as irregular, lobulated, round or oval. It is difficult to accurately quantify the irregularity of a mass. The oval or round shape of a mass will be determined by a elongation measure, which is defined as the ratio of the long axis to the short axis of the mass. In order to accurately determine the shape with the elongation measure, computer-extracted margin will be first smoothed with a morphological open filter. The elongation measures of a mass is calculated from the best fitted round/oval shape based on the smoothed margin of the mass. Although singularly, anatomic density of a mass may not be as powerful as margin or shape related features in distinguishing between benign and malignant masses, taken with the these features, the density assessment can be extremely useful For example, the evaluation of density of a mass is of great importance in diagnosing the masses in the non-spiculated category -- circumscribed, lobulated, indistinct, and obscured. Because the density of a mass is very difficult to accurately access, we introduce three density related measures to estimate the density of a mass lesion from different aspects, which is similar to the ones used by radiologists. They are the average gray-level of a mass, the contrast --the gray-level difference between the mass and its surrounding, and a texture measure -- standard deviation of the average gradient within a mass, which quantifies texture patterns such as veins, trabecular, or other structures that can be seen "through" from a low-density mass, but not a high density mass. A low-density mass tends to have a high value of the texture measure, and low values of average gray-level and contrast, whereas, a high-density mass tends to have a low value of the texture measure; and high values of average gray-level and contrast.

Results to date

We are investigating the potential usefulness of computer-aided diagnosis as an aid to radiologists in the characterization and classification of mass lesions in mammography. Ninety-five mammograms containing masses from 65 patients were digitized. Various features related to the margin, shape and density of each mass were extracted automatically from the neighborhoods of the computer-identified mass regions. Selected features were merged into an estimated likelihood of malignancy using three different automated classifiers. The performance of the three classifiers in distinguishing between benign and malignant masses was evaluated by receiver operating characteristic (ROC) analysis, and compared with those of an experienced mammographer and of five less experienced mammographers. Our computer classification scheme yielded an A_Z value of 0.94, similar to that of an experienced mammographer (A_Z=0.91) and statistically significantly higher than the average performance of the radiologists with less mammographic experience (A_Z=0.80). With the database we used, the computer scheme achieved, at 100% sensitivity, a positive predictive value of 83%, which was 12% higher than that of the experienced mammographer and 21% higher than that of the average performance of the less experienced mammographers at a *p*-value of less than 0.001. Thus, automated computerized classification schemes may be useful in helping radiologists distinguish between benign and malignant masses.

Development of computerized methods based on multiple views for enhanced mammographic interpretation.

Experimental methods

It is common for radiologists to utilize the correlation of certain lesions in two views in order to verify difficult and ambiguous cases and also to eliminate some possible false positive findings. We plan to investigate the relationship between the locations of lesions (and other landmarks) in breast images obtained with the CC and MLO views. If a suspicious region in one view is detected by our

CAD scheme, this relationship will be used to indicate the range of the potential locations of the corresponding region in another view. Since the variation of a location of a lesion in a breast can be very complex in two different views, we plan to employ an artificial network to learn the relationship between locations of lesions in two different views. This relationship will be used to eliminate some false positive findings and also to verify "true" lesions.

Initially each breast will be scaled to a "standard" breast size prior to coordinate determination and input to an ANN. This will be accomplished by scaling based on the distance from the nipple to the chest wall, and by fitting using the matching method employed in our bilateral-subtraction method. A simple way of determining the coordinates of a lesion employs the Cartesian coordinates of the lesion relative to the film edges. However, since the location of a breast image can be shifted easily by variation in the positioning of the breast in a mammography unit, we plan to investigate a more accurate method of determining the coordinates of the lesion in mammograms. We will employ a polar coordinate system based on the nipple position and the chest wall. For a CC view, the origin of the polar coordinates will be at the nipple position. The distance to the lesion will be measured from the nipple, and the angle will be determined from the line drawn from the nipple to the chest wall. For an MLO view, the origin of the polar coordinates will again be at the nipple position, and the angle will be determined from the line drawn from the nipple to the pectoral muscle.

A three-layer, feed-forward neural network will be used to correlate locations of the same lesion or the same landmarks in two different views. For each set of breast images, two neural networks will be used, namely, (1) a neural network for determining the range of the locations in MLO view when a lesion is found in CC view, and (2) another neural network for determining the range of locations in CC view when a lesion is found in MLO view. During training of the first neural network, the locations of lesions or landmarks in CC view will be entered to the first neural network's input units in terms of their coordinates, and the corresponding locations in MLO view will be given to the output units. The numbers of input units and output units will be equal to or greater than the total number of potential locations of lesions in all mammograms within a given breast size category in the respective view. For the second neural network, the locations in the MLO and CC views will be provided to units in the input and output layers, respectively.

For training each neural network, a unit in the input layer corresponding to a location of a lesion in polar coordinates in one view will have an input value of 1.0, and all other input units with a value of 0. A unit in the output layer corresponding to the location of the same lesions in another view will be given a desirable (target) output value of 1.0, and all other output units with a value of 0. We plan to use a "jack-knife" method for evaluating the performance of the trained neural network. With this method, a randomly-selected half of the data set will be used for training, and the other half will be used for testing. Results will be evaluated by ROC analysis, and the area under the ROC curve will be used as a measure of performance. We have used these methods successfully in the past for evaluating CAD and ANN. A number of parameters related to the neural networks, such as the number of hidden units and the number of iterations required for training, will be determined empirically based on ROC analysis. We plan to investigate the effect of the matrix size of the coordinate system and other parameters on the performance of the neural network in order to optimize the selection of many of the parameters that are involved. When the performance of the neural network for correlating the locations in two views is optimized, we plan to apply the trained neural networks to indicate the range of potential locations of the lesion in a view by entering the location of a finding in another view. The range of potential locations of the lesion will be determined from the distribution of output values in units in the output layer. A polynomial surface-fitting technique will be used to obtain a smooth distribution from the distribution of output values.

In the detection of masses by comparing a current mammogram with a previous one, the previous mammogram will be selected from recent exams obtained within three years of the time the current mammogram is obtained. Prior to the subtraction of two mammograms, the previous mammogram will be preprocessed in order to gray-level match it to the current mammogram. This preprocessing

step will involve gray level histogram modification and will only be performed if the difference in the average gray level within the breast region is greater than a predetermined value such as 150 in terms of a 10-bit range. We will limit this preprocessing in this way since our preliminary data indicates that the temporal subtraction method is sufficiently robust to be independent of slight gray level variations.

Prior to subtracting the current and the previous mammograms, breast borders in the two mammograms need to be matched reasonably well. We plan to initially employ a technique for alignment of breast borders that we have successfully applied previously to match two mammograms of the right and left breasts (75), based on the rigid transformation of a coordinates system by shifting and rotation. In order to align the two breast images, landmarks are used to establish the correspondence between the two images. Breast borders (discussed earlier) and nipple positions are used as such landmarks. The nipple position in each breast image is identified using a technique we developed (75) on the basis of the thicker skin line and greater subcutaneous parenchymal opacity that is present around the nipple. Image registration is accomplished by use of a "constrained feature-matching" technique that involves two steps: (1) determining a constrained correspondence between points (x,y locations along the borders); and (2) matching the established corresponding points of one image with those of the other image by use of a least-squares method for translation and rotation. The least-squares method used to find the "best" match between the two sets (i.e., 2 matrices) of (x,y) locations corresponding to the border points employs the solution of the "Orthogonal Procrustes Problem" obtained by Schonemann et al. (90). In order to compensate for possible computer error in the identification of nipple positions, the identified nipple position of each breast image is varied within a certain range and the matching procedure (described earlier) is repeated for each variation. The best registration is determined by finding the smallest minimized sum of squares of the residual matrix from all possible nipple-position variations. Using the resulting optimal alignment parameters, the corrected previous breast image is translated and rotated relative to the current breast image. A common region, defined as the region enclosed by both the current border and aligned previous breast border, is then determined and used as a common border.

For detection of masses, smaller matrix images of approximately 512 x 512 for the current and previous mammograms will be first prepared by subsampling the digitized mammogram of approximately 2k x 2k matrix. This reduction of matrix size has been shown to be useful for detection of masses in our previous study, since mass sizes are generally larger than 5 mm and the pixel size of approximately 0.4 mm is adequate for detection of masses. We plan to investigate linear and nonlinear subtraction techniques for detection of masses by comparison of the current mammogram at each view with the corresponding previous mammogram. With linear subtraction, the two mammograms are subtracted and then gray-level thresholding is performed to segment the current image into potential locations of masses. With nonlinear subtraction (similar to that used in our bilateral subtractiontechnique for comparing left and right breast images), gray-level thresholding is performed prior to subtraction. This initial thresholding eliminates some normal anatomic background from further analysis. A selected number of images thresholded with different cut-off gray levels is obtained from the current mammogram. Subtraction of ten sets of corresponding current and previous mammograms, each thresholded at ten different levels determined from the histogram, is performed to generate ten temporal-subtraction images. A linking process then accumulates the information into an image, called a run-length image, where the value of each pixel in the image indicates how often the corresponding location in the set of 10 subtraction images have gray levels above a particular cut-off gray value. The run-length image is thresholded to yield the suspicious areas and submitted for feature extraction similar to that discussed in section (1)(c) except different features will be selected as well as the structure and weights of a neural networks in order to customize the method for elimination of false positives. Our preliminary studies, involving an evaluation on temporal cases from 76 patients, yielded a sensitivity of approximately 75% at 3 false-positive detections per image. Note that there was no preselection of cases except that these patients had prior films and that no optimization for elimination of false positives was performed (i.e., the neural network from the bilateral subtraction method was used). Thus, we believe that optimization of the subtraction method and the feature selection will increase sensitivity and specificity.

Results to date

We have evaluated the potential benefit of incorporating a temporal subtraction scheme with our bilateral subtraction technique for improving the sensitivity of mass detection (106). A database of 79 cases was used, each of which contained a lesion in at least the current exam. Two methods for image registration of the temporal images were investigated: one used translation and rotation based on computer-determined skin lines and the other used a warping technique based on the cross-correlation of regions of interest located throughout the parenchyma. The characteristics of the false-positive detection sresulting form the bilateral subtraction and teom temporal subtraction were analysed. The distribution of the true positives and false positives were simlar despite the fact that many of the false positives resulting from the two schemes were in different locations in the breast parenchyma. At a false-positive rate of four per image, the combined (Logical OR) scheme detected 85% of the masses, which was 8% greater than the bilateral subtraction technique alone. Although further work is needed to reduce the false-positive rate, the combined use of bilateral and temporal subtraction methods shows potential for an improvement in sensitivity in the detection of masses.

Incorporation of the computer-vision methods with an Mammo/Icon mammographic review system for enhanced diagnosis.

Experimental methods

Mammo/Icon has been designed to compliment a radiologists normal reading patterns. The system is used to report mammographic findings, using either speech recognition technology, or mouse interaction with a graphical user interface. As findings are recorded, Mammo/Icon functions in the background, collecting potentially helpful images from a knowledge base. In this proposal, we plan to modify the Mammo/Icon system so that the features of the lesion in question are automatically determined. The system would then automatically retrieve images of similar characteristics for display to the radiologist. Along with the images, the computer would also indicate an estimate of the likelihood of malignancy.

The Mammo/Icon mammography image review system contains a detailed lexicon of mammography image features and associated scalar values which allow stratification of images by pre-defined and user defined criteria. This scheme will be expanded to allow retrieval of images based on CAD derived features including the geometric-based, intensity-based, and gradient-based features, as well as ANN outputs. The Mammo/Icon database is separately being modified for compatibility with BIRADS nomenclature. Separate pre-defined search strategies are used to set up each axis of retrieved images. Additional heuristics determine the order that images are presented in each array. When the quantitative CAD derived parameters are added to the descriptors of each reference image in the Mammo/Icon database, additional heuristics will be added to the axis ordering strategies to arbitrate conflicts with the existing system.

Currently, Mammo/Icon contains nearly 400 images. All images will be submitted to the CAD system for computerized characterization. The values obtained for characterization of the lesions will be added to the image descriptors in the Mammo/Icon database.

We will implement CAD and Mammo/Icon systems on existing hardware at both Yale University and the University of Chicago. Initially we will need to develop an hardware interface between CAD and Mammo/Icon. When a new index case is processed by the CAD system, it will automatically pass derived data to the Mammo/Icon search engine and generate a search of the image database. We will develop a sequential database search. The initial search of the Mammo/Icon database will be generated solely by automatically extracted features by the CAD system. A second pass search will be generated by features described by the radiologist during case reporting. A third iteration will integrate steps one and two. To accommodate these complimentary methods, the Mammo/Icon user

interface will be modified to allow additional axis display (and display of characterization targets from CAD).

Results to date

Dr. Swetts at Yale is upgrading the program for the Mammo/Icon in order to incorporate more current mammographic reference images. Once his software component is complete it will be integrated into the University of Chicago classification scheme.

Evaluation of the CAD methods for mammography

Experimental methods

Performance studies will be done using a database of mammographic cases that have a distribution of subtle cases of normal, benign and malignant masses. "Truth" concerning the presence and malignancy of masses will be established with the aid of expert mammographers, follow-up reports and surgical biopsy reports. Normal cases will be selected from patients who have had normal follow-up exams. Prior films will be obtained for each patient.

Performance will be examined by calculating the fraction of lesions detected (true-positive rate) and the number of falsely-reported areas per case. The clinical database for the performance evaluations will ultimately contain 300 cases (100 normal, 50 with spiculated lesions, 50 with architectural distortions, 50 with small early cancers, and 50 with circumscribed lesions). The performance of the methods will be determined in terms of self-consistency results and round-robin (leave-one-out) or jackknife methods. We have used such methods many times in the past in our evaluation of other computerized schemes . ROC curves will be obtained by fitting continuous output data from the computerized scheme (such as number of pixels in the Hough spectrum domain above threshold for each ROI) using the LABROC4 program (87,97,98). The area under the ROC curve (A_Z) will be used as an indicator of performance. Free-response ROC (FROC) analysis (99) and FROC-AFROC analysis (100) will be used in analyzing the data pertaining to localization of the abnormality. The ordinates of both FROC curves and AFROC curves are the fraction of lesions that are correctly localized by the observer. However, the abscissa of an FROC curve is the average number of false positives per image, whereas the abscissa of an AFROC curve is the probability of obtaining a false-positive image (i.e., an image containing one or more false-positive responses). We will fit an FROC curve to the performance data for each method being tested using Chakraborty's FROCFIT program (100). We have used this method in the past to fit mass detection data from our computerized scheme for the detection of masses using the bilateral subtraction approach and a single-image approach (68). The area A_1 under the AFROC curve, an alternative representation of the FROC curve, will be then used as the index with which to indicate performance.

Between the University of Chicago databases and Yale University Mammo/Icon database, we expect that 1000 radiographic lesions will be available for testing. Note that here the measure of performance will be the A_Z value (from ROC analysis) obtained in the task of distinguishing between malignant and benign lesions.

Results to date

Databases are continuously being collected. For mass detection, we have approximately 72 clinical cases of malignant masses. New data for the classification database includes the 72 malignant cases as well as 100 benign cases. The complete statistical evaluation will be performed at a later date when the databases are complete.

CONCLUSIONS

Computer-aided diagnosis has been successfully implemented in the clinical area for screening mammography using a prototype intelligent mammography workstation as a "second reader." The workstation provides for film digitization, image analysis, and display media for output of the computer aid. Introduction of the workstation did not result in an increase in callback rate. Results from the two-year evaluation period are promising and plans are being made for a longer-term clinical study.

We are continuing to investigate methods for increasing the sensitivity and specificity of the computerized detection method. We have found that a combined bilateral-image and single-image method inproves the sensitivity for detection.

We have evaluated the potential benefit of incorporating a temporal subtraction scheme with our bilateral subtraction technique for improving the sensitivity of mass detection. Although further work is needed to reduce the false-positive rate, the combined use of bilateral and temporal subtraction methods shows potential for an improvement in sensitivity in the detection of masses.

We will also incorporate information from both the CC and MLO views into the detection task. We have already incorporated information from both the MLO and CC views in the computerized classification of masses. We have shown that the computer-extracted features and the computer decision making process yield a classification performance that is similar to that of an experienced mammographer. The computer classification uses a hybird system incorporating both a rule-based system and an artificial neural network.

We are continuing to collect clinical databases for detection and classification. Upon completion of the database, statistical evaluation will be performed.

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